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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,598	06/27/2003	Roland Martin	4239-66190	7617

36218 7590 11/08/2006

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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 11/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/607,598	MARTIN ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 29-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21 and 29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 June 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Office Action mailed 8/9/06 has been vacated. A corrected Office Action follows. The references provided on PTO-892 of 8/9/06 will not be resent. In addition, the previously considered PTO-1449's of 2/17/04, 7/29/04 and 3/31/06 will not be resent. The reply period for this Office Action will start from the mailing date of this communication.

2.Applicant's election with traverse of Group I, directed to a method of treating a subject with multiple sclerosis in the reply filed on 5/26/2006 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden to search the subject matter of Group I with the subject matter of Group II. This argument is found to be persuasive and thus the rejection is withdrawn. Therefore, Groups I and II are rejoined. In addition, Applicant has added claims 32-34. Therefore, claims 1-21 and 29-34 are pending and are examined.

Priority

3. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Drawings

4. The drawings filed on 6/27/2003 are acknowledged. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because titles of Figures 4-6 are overlaid on top of the graphs. In addition, Figures 8A and 8B are not aligned. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new

drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Information Disclosure Statement

5. IDS submitted on 2/17/2004, 7/29/2004 and 3/13/2006 have been considered.

Specification

6. The use of the trademark Simulect, Zenapax, Antegren, Avonex, Betaseron, Copaxone, Prograf, Rapamune, Cellcept and Rebif has been noted in this application. These should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Objections

7. Claim 3 is objected to because of the following informalities: Claim recites that the IL-2 antagonist specifically binds the IL-21 receptor. However, the Office is assuming that this is a typographical error and IL-2 antagonist specifically binds the IL-2 receptor. Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 and 29-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8a. Claim 1 is rejected as vague and indefinite for reciting the term "ameliorating a sign" is not defined in the specification. Therefore the metes and bounds of these claims are unclear. Applicant on the specification (page 21, lines 5-9) indicates that the sign to be any abnormality indicative of disease, discoverable on examination or assessment of a subject. It is further stated that the sign is generally an objective indication of disease. It is stated that signs include, but are not limited to any measurable parameters such as tests for immunological status or the presence of lesions in a subject with multiple sclerosis. Because the specification provides no clear definition of what would constitute a "sign", the metes and bounds of the claim cannot be determined. It unclear what tests for immunological status is contemplated in claim 1. Claims 2-14, and 32 are rejected insofar as they are dependent on the rejected claim 1.

8b. Claims 11 and 12 are rejected as vague and indefinite for reciting that the treatment is also with interferon-beta 1a and interferon-beta 1b. However, claim1 from which these claims are dependent on recites that the "subject is administered a therapeutically effective amount of an IL-2 receptor antagonist in the absence of treatment with interferon beta, wherein the subject had failed to respond to a previous treatment with interferon beta". Thus, it is unclear if Applicant does indeed intend to use interferon-beta in subjects who have failed to respond previously with IL-2 antagonists (combination) in the instant invention.

8c. Claim 32 is drawn to an antibody that is a human monoclonal antibody. However, this claim depends on claim 4, which recites that the antibody is a humanized monoclonal antibody. Since, humanized monoclonal antibodies are normally rodent or mouse based antibodies, it is unclear how these antibodies can also be human monoclonal antibodies as recited in the instant invention.

Claim Rejections - 35 USC § 112, first paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9a. Claims 1-4, 7, 8, 10-18, 20, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of treating multiple sclerosis (ameliorating a symptom or by decreasing the number of contrast enhancing-lesions as evaluated by MRI), specifically by administering an IL-2 receptor antagonist that is an antibody (drawn to p55 or p75 subunits) composition, the specification does not reasonably provide enablement for the method of treatment by administering all IL-2 receptor antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 The factors to be considered when determining whether there is

sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claims 1-4, 7, 8, 10-18, 20, 29 and 30 are drawn to the method of treating multiple sclerosis (with ameliorating a symptom or by decreasing the number of contrast enhancing-lesions as evaluated by MRI) by administering an IL-2 receptor antagonist composition. However, Applicant's have only disclosed IL-2 receptor antagonist peptides and antibodies that bind to the subunits P55 and p75 (pages 8-9, 23-24). The specification as filed is insufficient to enable one skilled in the art to practice the claimed invention without an undue amount of experimentation because not all IL-2 receptor antagonists have been disclosed. IL-2 receptor antagonists include antibodies, peptides and small molecules or chemical compounds. Applicant has not identified a common structure responsible for the antagonist action but has identified the compound using a function (antagonist of IL-2 receptor). The usefulness of the method of treatment for multiple sclerosis recited in the claims is tied to the usefulness of IL-2 receptor antagonist disclosed (antibodies and peptides to the receptor subunits). Since, not all IL-2 receptor antagonists are disclosed and a common structure has not been identified, it is unclear how one skilled in the art can extrapolate the observations of the instant

invention to treat multiple sclerosis with all IL-2 receptor antagonists contemplated in the instant invention. In addition, the specification and the prior art have not disclosed a role for all IL-2 receptor antagonists in the treatment of multiple sclerosis.

If one skilled in the art is not guided as to the description of all IL-2 receptor antagonists, then the skilled artisan is also not guided as to how to use these antagonists in the methods for the treatment of multiple sclerosis. Since, there is inadequate guidance as to the nature of the invention, it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation to try various antagonists to IL-2 receptor to treat multiple sclerosis. In addition, because there are no working examples provided describing the use of all IL-2 receptor antagonists in the treatment of multiple sclerosis it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention.

In addition, there is no guidance provided for the mechanism associated with the treatment of multiple sclerosis recited in the claims. While mechanism is not required, it can allow extrapolation of enablement to non-exemplified embodiments. Since applicant has not provided any working examples to teach the method of treatment for multiple sclerosis by administering all IL-2 receptor antagonists either *in vitro* or *in vivo*, it would require an undue amount of experimentation to one of skill in the art to practice the invention commensurate in scope with the claims to treat multiple sclerosis by administering all IL-2 receptor antagonists.

Given the breadth of claims 1-4, 7, 8, 10-18, 20, 29 and 30 in light of the unpredictability of the art as determined by the lack of working examples, the level of

skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for a method of treating multiple sclerosis (ameliorating a sign or symptom or by decreasing the number of contrast enhancing-lesions as evaluated by MRI), specifically by administering all IL-2 receptor antagonist.

9b. Claims 1-4, 7, 8, 10-18, 20, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The claims are drawn to the method treating multiple sclerosis by administering IL-2 receptor antagonist. The specification discloses IL-2 receptor antagonist peptides and antibodies that bind to the subunits P55 and p75 (pages 8-9, 23-24)). However, the specification does not teach all IL-2 receptor antagonists. In addition, there are no structural attributes associated (or required) for the antagonistic function IL-2 receptor identified.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of IL-2 receptor antagonists, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1616.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the human sequence.

In this case, IL-2 receptor antagonist peptides and antibodies that bind to the subunits P55 and p75 (pages 8-9, 23-24) have only been disclosed. There is no identification of any particular structural requirement for the receptor antagonist. Applicant has described the compound by its function only. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Therefore, only disclosed IL-2 receptor antagonist peptides and antibodies that bind to the subunits P55 and p75, but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

9c. Claims 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

The recitation of "human monoclonal antibody" has no support in the specification. Although Applicant in the response filed 5/26/06 (page 5 of 7) indicates that the support for the claim language is found at page 25, lines 17-19 and page 24, lines 5-11, the antibodies disclosed at page 24, lines 5-11 disclose humanized and human antibodies not human monoclonal antibodies. In addition, the disclosure on page 25, lines 17-19 does not disclose human monoclonal antibody that specifically binds p55. The Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10a. Claims 1-9, 15-19, 21 and 29-31 rejected under 35 U.S.C. 103(a) as being unpatentable over Study of Zenapax in the treatment of multiple sclerosis (November, 2000 from PTO1449 of 2/17/2004) in view of Light et al. (U. S. Patent No. 6, 013, 256, PTO1449 of 2/17/2004).

Claims are drawn to a method treating multiple sclerosis by administering therapeutically effective amounts IL-2 receptor antagonists (daclizumab).

Study of Zenapax (2000) teaches use of Zenapax antibody in treating multiple sclerosis. The disclosure states that multiple sclerosis (MS) may be caused by an

abnormal immune response in which white blood cells called T lymphocytes attack the myelin sheath that covers nerves and parts of the spinal cord. It also teaches that Zenapax binds to protein receptors on lymphocytes, keeping them from interacting with interleukin-2, a substance necessary for their growth. Patients with multiple sclerosis who have had at least one relapse within 18 months of the start of the study and in whom interferon-beta treatment had not been successful were recruited in the study. Study was designed to administer the antibody by intravenous infusions over a 6-month period. The reference also teaches the use of MRI scans to evaluate the disease activity. It is hope that the study will address the effectiveness of the Zenapax antibody with respect to modifying the inflammatory activity in the brain of MS patients and inhibit autoimmune T lymphocytes that are involved in the disease process. However, this study does not disclose the specific dosage regimen for using Zenapax antibody.

Light et al. (U. S. Patent No. 6, 013, 256) discloses Zenapax (dacliximab) is a humanized anti-Tac murine monoclonal antibody that binds IL-2 receptor (columns 1 and 2). It teaches that this antibody specifically binds p55 (column 1, lines 16-20). The reference teaches the intravenous administration of the antibody at various antibody concentrations including 1.0 mg/kg and 1.5mg/kg (column 2, lines 39-60). Light et al. also discloses that the monoclonal antibody (murine anti-Tac) that binds to the p55 subunit of IL-2 receptor of human T and B lymphocytes, blocks the formation of the high-affinity IL-2 receptor and subsequent activation by IL-2 (column 1, lines 63-66). It also discloses antibody administration every other week and continuing until at least 8 weeks (column 3, lines 40-60, column 4 lines 29-30 and abstract). These studies were

conducted in patients with steroid-resistant acute graft-versus-host disease (column 2, lines 49-51), which is also an autoimmune disorder (as evidenced by Haskill et al. U. S. Patent No. 5, 817, 306) like multiple sclerosis.

Therefore, it would have been *prima facie* obvious at the time of the invention to modify the treatment methods of the study of Zenapax (2000) to treat multiple sclerosis as taught by the Light et al. using the therapeutic dosages (including those recited in the instant invention) of Zenapax used in treatment of the acute graft-versus-host disease. One of ordinary skill in the art would have been motivated to use the study of Zenapax to treat multiple sclerosis by administering daclizumab (Zenapax) because Light et al. disclose that daclizumab (a humanized antibody) binds to p55 subunit of IL-2 receptor of human T and B lymphocytes blocking the formation of the high-affinity IL-2 receptor and subsequent activation by IL-2. Further, there is reasonable expectation of success because Zenapax study teaches that IL-2 receptor antagonist daclizumab (Zenapax) can be used to treat multiple sclerosis patients in whom the interferon-beta treatment has not been successful because the antibody inhibits the autoimmune T lymphocytes that are involved in the multiple sclerosis disease process, thus ameliorating a sign or symptom of multiple sclerosis in a subject. Therefore, the instant invention is *prima facie* obvious over Study of Zenapax in the treatment of multiple sclerosis (November, 2000 from PTO1449 of 2/17/2004) in view of Light et al. (U. S. Patent No. 6, 013, 256, PTO1449 of 2/17/2004).

10b. Claims 1, 10-15 and 20 rejected under 35 U.S.C. 103(a) as being unpatentable over Study of Zenapax in the treatment of multiple sclerosis (November, 2000 from PTO1449 of 2/17/2004) in view of Light et al. (U. S. Patent No. 6, 013, 256, PTO1449 of 2/17/2004) and Goodin (2000).

Claims are drawn to a method treating multiple sclerosis by administering therapeutically effective amounts IL-2 receptor antagonists (daclizumab) and interferon-beta. In addition, claims are also drawn to evaluating the disease using MRI.

The teachings of the Study of Zenapax and Light et al. have been described above in paragraph 9a. However, these teachings do not disclose the use MRI to evaluate the lesions (disease progression) and the use interferon-beta in the treatment of multiple sclerosis. In addition, the references also do not teach relapsing-remitting multiple sclerosis (RRMS) and progressive multiple sclerosis. Furthermore, the references do not disclose the combination therapy (interferon-beta and IL-2 receptor antagonist).

Goodin teaches the use of MRI to objectively measure the pathology of multiple sclerosis (page 657, 3rd paragraph). It also discloses that the MRI measures attack rate (e.g., new lesions, enhancing lesions, or combined unique active lesions) has been used to support the clinical attack rate (page 657, 3rd paragraph). Goodin also discloses the uses of interferon-beta 1a and 1b on Table I. In addition, the reference also teaches relapsing-remitting multiple sclerosis (RRMS) and progressive multiple sclerosis (page 656, 3rd paragraph) are different forms MS with different clinical progression. Goodin

also argues for the use of combination therapies to control MS (page 667, 2nd paragraph).

Therefore, it would have been *prima facie* obvious at the time of the invention to modify the treatment methods of the study of Zenapax (2000) and Light et al. with the teachings Goodin to treat multiple sclerosis. One of ordinary skill in the art would have been motivated to use the modified methods of the study of Zenapax and Light et al. to treat multiple sclerosis and evaluate the efficacy of treatment by MRI (looking at the number of contrast enhancing lesions) as disclosed in Goodin because the reference teaches the use of MRI to look at the attack rate to study the pathology of MS (page 657, 3rd paragraph). There is a reasonable expectation of success because Goodin teaches the use of MRI to objectively measure the pathology of multiple sclerosis (page 657, 3rd paragraph). Both relapsing-remitting multiple sclerosis (RRMS) and progressive multiple sclerosis, which are different forms of MS (see page 656) are also expected to be treated in with Zenapax. In addition, one of ordinary skill in the art would have been motivated to use combination therapy of including daclizumab antibody with either interferon-beta 1a or interferon-beta 1b described in Goodin to treat multiple sclerosis because the reference teaches that combination therapies will be used increasingly in the future to control the biological activity. Further, there is reasonable expectation of success for using combination therapy based on the analogy to the experience in oncology (Goodin, page 665). Therefore, the instant invention is *prima facie* obvious over Study of Zenapax in the treatment of multiple sclerosis (November, 2000 from

PTO1449 of 2/17/2004) in view of Light et al. (U. S. Patent No. 6, 013, 256, PTO1449 of 2/17/2004) and Goodin (2000).

10c. Claims 1, 10-15 and 20 rejected under 35 U.S.C. 103(a) as being unpatentable over Study of Zenapax in the treatment of multiple sclerosis (November, 2000 from PTO1449 of 2/17/2004) in view of Light et al. (U. S. Patent No. 6, 013, 256, PTO1449 of 2/17/2004) and Haskill et al. (U. S. Patent No. 5, 817, 306).

Claims are drawn to a method treating multiple sclerosis by administering therapeutically effective amounts IL-2 receptor antagonists (a human monoclonal antibody).

The teachings of the Study of Zenapax and Light et al. have been described above in paragraph 9a. However, these teachings do not disclose the use of human monoclonal antibody. Haskill et al. disclose the preparation of human monoclonal antibody to IL-1 receptor from lymphocytes sensitized with IL-1 receptor, or with cells that bear the same, either *in vivo* or *in vitro* by immortalization of antibody-producing hybrid cell lines, thereby making available a permanent source of the desired antibody (column 9, lines 1-6). The reference also discloses the use of the IL-1 receptor antagonist to treat autoimmune diseases such as graft versus host disease (abstract).

Therefore, it would have been prima facie obvious at the time of the invention to modify the treatment methods of the study of Zenapax (2000) and Light et al. with the teachings of Haskill et al. to generate human monoclonal antibodies to p55 sub unit of IL-2 receptor to treat multiple sclerosis. One of ordinary skill in the art would have been

motivated to use the methods Haskill et al to generate human monoclonal antibodies directed to p55 sub unit of IL-2 receptor to treat MS because the reference teaches the generation of human monoclonal antibodies to IL receptors treat autoimmune related diseases (abstract) and because Light et al. teaches that humanized forms of the antibodies are less or non-immunogenic in human patients (see columns 2, 5-7). There is a reasonable expectation of success of generating human monoclonal antibodies to IL-2 receptor because Haskill et al. was successful in generating a human monoclonal antibody to IL-1 receptor. Further, there is reasonable expectation of success for using human monoclonal antibodies directed to p55 subunit of IL-2 receptor to treat MS because study of Zenapax teaches that IL-2 receptor antagonist daclizumab (Zenapax, a humanized monoclonal antibody) can be used to treat multiple sclerosis patients in whom the interferon-beta treatment has not been successful and also because it will the reduce antigenic effect generated to foreign antibodies in the patients. Therefore, the instant invention is *prima facie* obvious over Study of Zenapax in the treatment of multiple sclerosis (November, 2000 from PTO1449 of 2/17/2004) in view of Light et al. (U. S. Patent No. 6, 013, 256, PTO1449 of 2/17/2004) and Haskill et al. (U. S. Patent No. 5, 817, 306).

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-21 and 29-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 20 of copending Application No. 10/519, 311. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-21 and 29-34 of the instant application is drawn to methods of treating a subject with multiple sclerosis who was unresponsive to IFN-β treatment, wherein said method comprises administering an IL-2R antagonist, which includes an antibody that binds IL-2R, and includes anti-Tac antibody daclizumab (Zenapax). Claim 20 Application No. 10/519, 311 is drawn to a method of treating a subject with multiple sclerosis who was unresponsive to treatment with IFN-β alone, wherein said method comprises administering a therapeutically effective dose of anti-Tac antibody.

It would be obvious to a person of ordinary skill the art to practice the method of claims 1-21 and 29-34 of the instant application by using the methods set forth in the '311 application. Both applications recite treatment of multiple sclerosis patients who did not respond to treatment with IFN-β, and thus are seeking to treat the same patient

population. Furthermore, both applications are drawn to methods of administering an IL-R antagonist, and both applications recite the use of antibodies such as anti-Tac/daclizumab, that specifically bind the IL-2R. Although, claim 20 of the '311 application does not recite any specific doses or timing of administration, one of ordinary skill in the art would easily be able to optimize these variables and practice a method that is commensurate in scope with the methods set forth in the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

12. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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JSS
Art Unit 1647
October 30, 2006

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